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Margaret Crews

PHARMACOGENOMICS: TAILORING THE DRUG APPROVAL PROCESS FOR DESIGNER DRUGS

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INTRODUCTION

Pharmacogenomics is the practice of tailoring drugs to particular genetic profiles, with the ambition of reducing instances of adverse reactions and ensuring optimal treatment.[1] Owing its existence in part to the success of the Human Genome Project (HGP)[2] the pharmacogenomic movement grew as the relationship between genetics and a person's health became increasingly relevant in understanding disease.[3] The entry of pharmacogenomics into drug therapy is greatly anticipated largely due to the positive impact it will have on drug therapy and development, but substantial hurdles exist.[4]

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[*] J.D. 2008. The Catholic University of America, Columbus School of Law; B.A. 2003, Kenyon College. The author would like to thank Professor Kelly for acting as an advisor during the writing period, as well as the Journal of Contemporary Health Law and Policy staff for their editorial support.

1. Janet Woodcock, *FDA Policy on Pharmacogenomic Data in Drug Development*, 66 LA. L. REV. 91, 92 (2005) ("Pharmacogenomics, is the science of correlating drug responses to genetic data—meaning the generation of gene or gene expression data that correlate genes and observed drug responses."); *see also*, Dep't of Energy, Office of Sci., Human Genome Program, Pharmacogenomics, http://www/ornl.gov/sci/techresources/Human_Genome/medicine/pharma.shtml (last visited Mar. 22, 2008) [Hereinafter Human Genome Program].

2. Human Genome Program, *supra* note 1.

3. *Id.*

4. *Id.* (The anticipated goals of pharmacogenomics are listed by HGP as: more powerful drugs; effective treatment immediately as opposed to "trial-and-error" prescriptions; more accurate methods of determining appropriate drug dosages; advanced screening for disease; better vaccines; better, cheaper drug trials as pharmacogenomics companies will be able to discover potential therapies through drug trials for specific genetic populations; and, thus, a decrease in overall health care costs. Barriers and potential pitfalls of pharmacogenomics are described by the HGP as: time consuming in that finding gene variations that affect drug response is not a quick process; certain gene variations may preclude the use of certain drugs, thus reducing treatment options rather than increasing treatment options; the preclusion of many gene variations may become a

One of the challenges facing the development of pharmacogenomics is that it must occur within the Food and Drug Administration's (FDA) regulatory framework. This framework has necessarily evolved as drug therapy has advanced.[5] Regardless of changes in methodology, the twofold mission of the FDA, to protect public health by assuring the safety, efficacy, and security of drugs that enter the market and to ensure that advanced and innovative new drugs reach the public in a timely manner, remains steadfast.[6] Despite reform, the FDA is consistently criticized by consumer

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disincentive for drug companies to produce multiple pharmacogenomic products as the financial incentive may be lowered; and, finally, pharmacogenomics requires doctors and providers to develop and maintain a greater understanding of genetics than was previously necessary); *see also* Teresa Kelton, *Pharacogenomics: The Re-Discovery of the Concept of Tailored Drug Therapy and Personalized Medicine*, 19 HEALTH LAWYER 3 (2007).

5. *See generally* Howard Markel, *Why America Needs a Strong FDA*, 294 JAMA 2489, 2489 (2005); U.S. Food & Drug Admin., New Requirements for Prescribing Information, www.fda.gov/cder/regulatory/physlabel/default.htm (last visited Jan. 29, 2007) (The FDA revised the prescription drug format in 2006 in an effort to improve the accessibility of drug information).

6. The FDA introduced the "Critical Path Initiative" on March 16, 2004, an "effort to stimulate and facilitate a national effort to modernize the sciences through which FDA-regulated products are developed, evaluated and manufactured." U.S. FOOD & DRUG ADMIN., FDA'S CRITICAL PATH INITIATIVE—SCIENCE ENHANCING THE HEALTH AND WELL-BEING OF ALL AMERICANS (Jan. 2007), http://www.fda.gov/oc/initiatives/criticalpath/initiative.html. Despite the FDA's concern that drug development was not reaching its full potential, drug approval rates have peaked due to the Prescription Drug User Fee Act. *See* Phil B. Fontanerosa et al., *Postmarketing Surveillance—Lack of Vigilance, Lack of Trust*, 292 JAMA 2647, 2647 (2004) (stating that median drug approval times had been reduced from 27 months in 1993 to 14 months in 2001); *see also* Douglas J. Pisano, FDA REGULATORY AFFAIRS: A GUIDE FOR PRESCRIPTION DRUGS, MEDICAL DEVICES, AND BIOLOGICS 12-13 (Douglas J. Pisano & David Mantus eds., CRC Press) (2004) [hereinafter FDA REGULATORY AFFAIRS] ("[A]pproval rates have increased from approximately 50% to nearly 80% and the review times have decreased to under 15 months for most applications."); *but see* Robert Oldham, Assoc. Dir., Singletary Oncology Ctr., Remarks at the Manhattan Institute Conference Series: Medical Progress and the FDA: Our Future in the Balance (June 3, 2002) *available at* http://www.manhattan-institute.org/html/mics8.htm [hereinafter Oldham] (reporting that between 1990 and 2002 the number of drugs approved by the FDA had not changed significantly and while the approval time grew shorter, the total drug development time has increased by more than half because of new rules and paperwork required by the FDA and that the total cost of development has also increased).

advocates for being too closely connected with drug manufacturers and for failing to adequately follow approved drugs once they have entered the market.[7] Proponents of pharmaceutical development criticize the FDA as stalling innovation and alienating free market principles.[8] The successful entry of pharmacogenomics into the practice of medicine will require the FDA to address many of its shortcomings without chilling advancements in the modernizing and changing field of drug therapy.[9] The ability of pharmacogenomics to meet this challenge will require legislative action to motivate pharmaceutical companies, the FDA, and medical professionals to work together in creating a safe, effective, and modern drug market.

This comment addresses the FDA's struggle to realize the goals of its mission statement, which include lofty ambitions for the prompt availability of innovative, effective, and safe drugs.[10] The entry of pharmacogenomics into mainstream medicine will create novel concerns that further tax the FDA and hinder medical advancement if not anticipated through appropriate legislation.[11] It is imperative to address the FDA's current shortfalls with

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7. *See* Fontanerosa et al., *supra* note 6, at 2647.

> The inadequacies of the postmarketing surveillance system . . . for ensuring safety are well known and include: reliance on voluntary reporting of adverse events by physicians and other health care professionals; poor quality of submitted reports, often with inadequate documentation and detail; underreporting of adverse outcomes with capture of only a small fraction of adverse events that actually occur; difficulty in calculating rates of adverse events, together with unreliable denominator data on exposure; limited ability for spontaneous reports to establish causal relationships; and difficulty in determining whether the adverse event resulted from the drug or the disease it was intended to treat.

Id.; see also Sheila R. Shulman & Andrea Kuettel, *Symposium on Health Care: Drug Development and the Public Health Mission: Collaborative Challenges at the FDA, NIH, and Academic Medical Centers*, 53 BUFFALO L. REV. 663, 666 (2005).

8. *See* Richard Epstein, *Regulatory Paternalism in the Market for Drugs: Lessons from Vioxx and Celebrex*, 5 YALE J. HEALTH POL'Y L. & ETHICS 741, 748 (2005).

9. Woodcock, *supra* note 1, at 94.

10. U.S. Food & Drug Admin., FDA's Mission Statement, http://www.fda.gov/opacom/morechoices/mission.html (last visited Mar. 22, 2008).

11. *See* Woodcock, *supra* note 1, at 94.

> From a public policy standpoint, the goal is to advance the science and to move it along as quickly as possible in a responsible manner because it has such promise to advance

legislation that anticipates pharmacogenomics. This comment first addresses the current system at the FDA, then it focuses on pharmacogenomics and their impact, reviews legislative responses to previous concerns in drug development and the applicability of such responses in anticipation of pharmacogenomics, and this comment finally concludes with recommendations for legislative solutions. These recommendations call for development incentives, continued improvement in the area of post-market surveillance of drugs, and increased access to information.

I. FDA: CURRENT STATE OF AFFAIRS

At present, the FDA is responsible for the approval of new drugs, as well as the continued surveillance of drugs to identify new risks and hazards after they have entered the market.[12] Accordingly, it is important to address both the pre-approval period and the post-approval period when considering current concerns as well as potential solutions. Consistent with its mission, the FDA has established various programs and initiatives to help increase the rate of drug development so that it maintains an even pace with scientific advances and discoveries.[13] To fulfill its role in advancing public health, the FDA must delicately balance its interest in keeping unsafe drugs off the market with its interest in encouraging innovation.[14]

A. Drug Approval Process

Pursuant to the Federal Food, Drug, and Cosmetic Act (FDCA), prior to approval for marketing in the United States, all new drugs are subjected to

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therapeutics and to improve human health . . . . We *need* appropriate legal and regulatory policies put in place to allow things to move forward responsibly. Moreover, we have to integrate our existing—and this is what is often very challenging—regulatory and legal framework with this new science. As a new science emerges, the laws and policies crafted in an earlier time for an earlier type of information, data, or science often become awkward entanglements.
Id.

12. *See* U.S. Food & Drug Admin., *supra* note 10.

13. *See id.*

14. Markel, *supra* note 5, at 2491 ("Throughout its history, the FDA has had to negotiate a hard line between its charge of protecting the American public based on scientific evidence and the pressing needs or desires of business interests."); *see generally* Epstein, *supra* note 8.

a lengthy and expensive investigative process administered by the FDA.[15] The Center for Drug Evaluation and Research (CDER) reviews the applications for drug approval and monitors approved drugs that have reached the market.[16] The CDER largely finances its reviews through prescription drug user fees (PDUFs), which pharmaceutical companies pay to the FDA with the specific purpose of accelerating the drug approval process.[17]

In practice, FDA approval starts with a preclinical investigation to ensure that the potential drug can be safely tested on humans, after which an investigational new drug application (INDA) must be submitted to the FDA.[18] If the FDA does not object to the application, a clinical study protocol must be submitted and approved by an Institutional Review Board (IRB).[19] The clinical investigation of a new drug has several phases: Phase I includes a small, brief study of human subjects; Phase II includes controlled studies with human subjects who have the disease or condition being treated; and Phase III includes larger studies that are meant to discover any unanticipated adverse effects on individuals.[20] In its final phase, a New Drug Application (NDA) is submitted to the FDA.[21] The NDA must include an extensive collection of information consisting of all data collected during the trials as well as labeling, manufacturing plans, and a risk-benefit analysis

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15. FDA REGULATORY AFFAIRS, *supra* note 6, at 11–12; *see also* Joe DiMasi, Dir., the Tufts Ctr. for the Study of Drug Dev., Remarks at the Manhattan Institute Conference Series: Medical Progress and the FDA: Our Future in the Balance (June 3, 2000) [hereinafter DiMasi] (stating that the range for out of pocket research and development costs for pharmaceutical companies was between $354 million and $558 million per drug and the range for capitalized costs was between $650 million and $1 billion); Oldham, *supra* note 6.

16. U.S. FOOD & DRUG ADMIN., IMPROVING PUBLIC HEALTH, CENTER FOR DRUG EVALUATION AND RESEARCH (2003), http://www.fda.gov/opacom/factsheets/justthefacts/3cder.pdf.

17. U.S. Food and Drug Admin., Prescription Drug User Fees—Overview, http://www.fda.gov/oc/pdufa/overview.html (last visited Mar. 23, 2008).

18. FDA REGULATORY AFFAIRS, *supra* note 6, at 8–9.

19. *Id.* at 9–10.

20. *Id.* at 10–11.

21. *Id.* at 11.

of the new drug.[22] In addition to showing that the drug is safe for use, the NDA must also show that there is "substantial evidence" that the product will have its intended effect.[23] "Substantial evidence" is defined as "[a]dequate and well controlled investigations including clinical investigations, by experts qualified by scientific training and experience to evaluate the effectiveness of the drug involved, on the basis of which it could fairly be concluded by such experts that the product will have the effect it purports to have."[24] In 2004, due to questions about drug approval standards, the FDA implemented an adjudicatory program in which differences of professional opinion between the FDA and outside experts could be reviewed, drug safety/risk management consultations with other experts and agencies were authorized, and management guidelines for pharmaceutical companies to aid in identifying and assessing safety risks were published.[25]

The FDA must decide that a drug is "safe and effective" to treat a particular condition before approving it.[26] To determine whether a drug is "safe and effective," the FDA may apply a cost-benefit analysis. Since the consumer's opinion or desire is given little consideration in such an analysis, some commentators perceive this as both "tentative" and "paternalistic."[27] Concerns that the FDA stifles innovation and development or, conversely, that the FDA is too deeply involved with the pharmaceutical companies to

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22. *Id.*

23. 21 U.S.C. § 355(d) (2000).

24. *Id.*

25. Press Release, Lester M. Crawford, Acting Comm'r, U.S. Food & Drug Admin., FDA Acts to Strengthen the Safety Program for Marketed Drugs (Nov. 5, 2004), http://www.fda.gov/bbs/topics/news/2004/NEW01131.html.

26. 21 U.S.C. § 355(d).

27. Richard Epstein has expressed his disagreement with the FDA's cost-benefit analysis:

> Often, [the FDA] relies on cost-benefit analyses that can only be termed, at best, tentative and, at worst, primitive. Its entire effort to make better judgments on what treatments should be used and why smacks of an unthinking paternalism that reveals its own institutional shortcomings, as well as those of its critics who plump for stricter regulation.

Epstein, *supra* note 8, at 747.

make objective decisions about drug safety, are ever-present in critiques of the approval process.[28] Although the FDA approval process may eliminate some risks, adverse events will inevitably occur after approval and outside the controlled trial setting.[29]

B. Post-Market Surveillance of Drugs

The FDA sponsored a 2004 Institute of Medicine study of the drug safety system, which reported that the CDER devoted less time and fewer resources to post-market surveillance of drugs; rather, it devoted most of its resources to the approval of new drugs.[30] This finding may be correlated to the large amount of CDER funding derived from Prescription Drug User Fees (PDUFs).[31]

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28. Markel, *supra* note 5, at 2490–91.

> Early during Reagan's first term, FDA budgets were severely cut, legal investigations were canceled, and new policies were developed that would overload workers with paperwork rather than allowing them to devote more time to pursuing errant pharmaceutical companies and other businesses. This trend progressed through the early 1990s, and while the deregulation slide was curtailed somewhat during the Clinton years, critics increasingly complained that the FDA was developing alliances that were too close to the industries it was charged with regulating. The rationale for these changes was the popular argument that the FDA inhibited business profits and therefore inhibited research and development, cost too much money to operate, and failed to uphold its primary missions.

Id.

29. *See Ensuring Drug Safety: Where do We Go From Here?: Hearing on Drug Safety Before the S. Comm. on Health, Education, Labor, and Pensions,* 109th Cong. 40–47 (2005) (statement of Dr. Bruce Psaty, Co-director of the Cardiovascular Health and Research Unit and professor of medicine, epidemiology, and health services, University of Washington) [hereinafter Psaty]; *see also* Michael Friedman et al., *The Safety of Newly Approved Medicines*, 281 JAMA 1728, 1732 (1999) ("[D]rug approvals are made on the basis of limited information and more inevitably learned as a drug becomes widely used.").

30. *See The Future of Drug Safety: Promoting and Protecting the Health of the Public*, THE INST. OF MED. OF THE NAT'L ACADEMICS, Sep. 22, 2006, http://www.iom.edu/ CMS/3793/ 26341/37329.aspx.

31. Gregory D. Curfman et al., *Blueprint for a Stronger Food and Drug Administration*, 355 NEW ENG. J. MED. 1821 (2006).

In an effort to promote drug safety in 2005, the FDA created and authorized a Drug Safety Oversight Board to review and analyze adverse drug event reports, drug use data, healthcare administrative data, epidemiologic and observation studies, clinical trials, and other surveillance systems.[32] In 2005, there were 5 safety drug recalls, 109 safety alerts for drugs, 25 to 70 safety-related labeling changes per month, and over 460,000 reports of adverse drug events.[33] A 2006 United States Government Accountability Office (GAO) study reported that improvement was still needed in the FDA's post-market oversight programs.[34] The study attributed the FDA's insufficient post-market surveillance largely to a lack of effective organization and oversight within the FDA and the limited nature of available data.[35] One oversight program, MedWatch, exemplifies some of the frustrations that the FDA faces in tracking drugs that have reached the market. MedWatch encourages doctors to voluntarily report adverse events.[36] However, the program is often labeled inadequate because adverse events are under-reported, and reported events fail to produce adequate and reliable information.[37]

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32. U.S. FOOD & DRUG ADMIN., CENTER FOR DRUG EVALUATION AND RESEARCH, REPORT TO THE NATION 2005: IMPROVING PUBLIC HEALTH THROUGH HUMAN DRUGS 4 (2005).

33. *Id.* at 35–43.

34. U.S. GOV'T ACCOUNTABILITY OFFICE, DRUG SAFETY: IMPROVEMENT NEEDED IN FDA'S POSTMARKET DECISION-MAKING AND OVERSIGHT PROCESS (2006) [hereinafter GAO DRUG SAFETY REPORT].

> FDA lacks clear and effective processes for making decisions about, and providing management oversight of, postmarket safety issues. The process has been limited by a lack of clarity about how decisions are made and about organizational roles, insufficient oversight by management, and data constraints. GAO observed that there is a lack of criteria for determining what safety actions to take and when to take them.

Id.

35. *Id.*

36. U.S. Food & Drug Admin., MedWatch: The FDA Safety Information and Adverse Event Reporting Program, Voluntary Reporting by Health Professionals, http://www.fda.gov/medwatch/report/hcp.htm (last visited Feb 22, 2008).

37. *See* Fontanarosa et al., *supra* note 7, at 2647; *see also* Psaty, *supra* note 29 (finding that adverse events are often under-reported, perhaps largely due to fear of legal

Public recalls of drugs and well-publicized lawsuits resulting from adverse drug reactions have added fuel to the movement for reforming the FDA's surveillance of approved drugs.[38] Anticipating the renewal of the Prescription Drug User Fees Act in 2007, drug companies and the FDA engaged in talks to determine how to best restructure the program.[39] In January of 2007, the FDA published its recommendations for reauthorization of the PDUF program.[40] The recommendations include an $87.4 million increase in user fee collections, of which $29.3 million would be put towards ensuring post-market safety of medications.[41] The Senate and the House passed similar bills in the summer of 2007.[42] Ultimately, the bill approved by Congress and signed into law by the president, the Food and Drug Administration Amendments Act of 2007 (FDAA), gave the FDA new tools for monitoring drug safety.[43] The FDAA grants the FDA the authority to require safety studies by drug companies, to limit distribution of certain drugs, and to require label changes.[44]

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ramifications, and those adverse events that are reported fail to provide the level of documentation necessary to definitively attribute causation to the drug).

38. *See generally* Gardiner Harris, *Regulation Redefined: The FDA Shifts Focus; At FDA, Strong Ties and Less Monitoring*, N.Y. TIMES, Dec. 6, 2004, at A1, *available at* http://www.nytimes.com/2004/12/06/health/06fda.html?ex=1164949200&en=d31b327e2d66f4ed&ei=507; Friedman, *supra* note 29, at 1728 ("Between September 1997 and September 1998, five prescription medications were removed from the market because of unexpected adverse reactions. These actions raised questions about whether unsafe products were reaching the US market because the drug approval process had been expedited under the Prescription Drug User Fee Act of 1992.").

39. Jeffrey Young, *Democratic Leaders Eye FDA Reform*, THE HILL, Nov. 6, 2006, *available at* http://thehill.com/thehill/export/TheHill/News/TheExecutive/111606_fda.html.

40. Prescription Drug User Fee Act, Public Meeting Notice, 72 Fed. Reg. 9, 1743, 1745–52 (Jan. 16, 2007).

41. *Id.* at 1746–47.

42. S. 1082, 110th Cong. (2007); H.R. 2900, 110th Cong. (2007).

43. *See* Food and Drug Administration Amendments Act of 2007, Pub. L. No. 110-85, 121 Stat. 823 (2007).

44. *Id.*

Previously, the FDA could not require the post-market studies of drugs and rarely required a pharmaceutical company to remove a drug from the market, nor could it require continued availability or sale of a drug.[45] While the FDA could request pharmaceutical companies to continue collecting data and performing medical trials after drug approval,[46] this scheme has proved ineffective in the past due to lack of compliance and under-reporting.[47] Perhaps the most accurate post-approval research was initiated by pharmaceutical companies themselves in order to target future uses of a drug, although many may have avoided reporting negative information by discontinuing studies with questionable results.[48] In 2006, the GAO recommended that Congress expand the FDA's authority to require drug sponsors to conduct post-market studies.[49] And as of October 1, 2007, if the FDA is made aware of "new safety information," it may require pharmaceutical companies to conduct postapproval studies or trials.[50] "New safety information" is defined as

> information derived from a clinical trial, an adverse event report, a postapproval study, or peer-reviewed biomedical literature; data derived from the postmarket risk identification and analysis system; or other scientific data deemed appropriate by the Secretary about—a serious risk or any unexpected serious risk associated with the drug that the Secretary has been aware of . . . .[51]

The FDAA also authorizes the FDA to order a label change if new safety information becomes available that the FDA believes should be included in

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45. GAO DRUG SAFETY REPORT, *supra* note 34, at 4.

46. *See* Psaty, *supra* note 29.

47. *Id.* ("Pharmaceutical companies often promise post-marketing clinical trials as a condition of approval. In practice, however, more than half of these promised studies . . . have not been started."); *see also* Fontanarosa et al., *supra* note 7, at 2647.

48. *See* Psaty, *supra* note 29; *see also* Fontanarosa et al., *supra* note 7, at 2649 (indicating that where results are seemingly detrimental to the company, it is likely that the study will be discontinued and any reports of the findings will be downplayed).

49. GAO DRUG SAFETY REPORT, *supra* note 34, at 6.

50. Food and Drug Administration Amendments Act of 2007, Pub. L. No. 110-85, 121 Stat. 923 (codified as amended at 21 USC § 355(o)(3) (2007)).

51. *Id.* at 121 Stat. 927 (codified as amended at 21 U.S.C. § 355-1).

the label.[52] The requirement of "Risk Evaluation and Mitigation Strategies" (REMS) was also included in the FDAA.[53] REMS are plans submitted by drug applicants when it is determined by the FDA that a REMS plan is necessary to mitigate the risks of some drugs.[54] The FDA may require a REMS plan at the time of drug approval or after drug approval when new safety information becomes available.[55]

C. Labeling and Preemption

Of particular relevance when considering the unpredictable nature of new drugs, is the proliferation of off-label prescribing by doctors, arguably a practice that has been encouraged by the FDA.[56] Off-label prescribing is the practice of prescribing an FDA-approved drug for an unapproved use, for example prescribing an asthma medication for pulmonary disease.[57] The support for off-label use is widespread in the medical community as doctors, pharmaceutical companies, and the federal government acknowledge the potential benefits of such prescribing practices.[58] The case for off-label prescribing is undeniably strong as the practice gives credence to a doctor's

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52. *Id.* at 121 Stat. 923 (codified as amended at 21 USC § 355(o)(4)(A)).

53. *Id.* at 121 Stat. 926 (codified as amended at 21 USC § 355-1).

54. *Id.*

55. *Id.*

56. James Beck & Elizabeth Azari, *FDA, Off-Label Use, and Informed Consent: Debunking Myths and Misconceptions*, 53 FOOD & DRUG L.J. 71, 79 (1998) ("'[U]napproved' or more precisely 'unlabelled' uses may be appropriate and rational in certain circumstances . . . .") (quoting 12 FDA DRUG BULLETIN 4–5 (1982)); *id.* at 103 (finding that current law allows pharmaceutical companies to promote off-label uses to providers of health care); Mitchell Oates,Note, *Facilitating Informed Medical Treatment Through Production and Disclosure of Research into Off-Label Uses of Pharmaceuticals*, 80 N.Y.U. L. REV. 1272, 1280–81 (2005) ("Indeed, many believe a hands-off approach provides a desirable level of freedom, allowing practitioners to pursue innovative treatment strategies, and facilitating the discovery of new uses.").

57. *See* Oates, *supra* note 56, at 1273.

58. *See* Beck & Azari, *supra* note 56, at 79–80 (finding that "[o]ff-label use is not only legal and ethical, but it is a common and integral feature of medical practice" and citing estimates finding that prescriptions for off-label uses may account for "as high as 60%" of "the approximately 1.6 billion prescriptions written each year").

autonomy in treating his/her patient, avoids the burden of seeking FDA approval for every usage of a particular drug, and, most importantly, often helps suffering individuals.[59]

Recently, the FDA revised its drug labeling policies in an effort to create a more physician-friendly format but sparked some controversy due to language in the preamble. The preamble asserted that state drug labeling laws were preempted by the FDA's labeling requirements thereby potentially eliminating certain tort suits against pharmaceutical companies.[60] The preemption language in the preamble of the FDA's final labeling rule, which took effect on June 30, 2006, did not go unnoticed by critics.[61] The FDA claims the authority to preempt state labeling requirements as "the expert Federal public health agency charged by Congress with ensuring that drugs are safe and effective."[62] The FDA asserts further that the drug approval process is rigorous and results in "authoritative conclusions" as to the effective uses of a drug, which are adequately described along with any risks and benefits of the product in an approved label.[63] The FDA explains that state laws on labeling conflict with the FDA's designation as the expert in drug regulation, thus preemption is necessary.[64] The FDA argues that varied labeling requirements may have detrimental consequences for the

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59. *See* Steven Salbu, *Off-Label Use, Prescription, and Marketing of FDA-Approved Drugs: An Assessment of Legislative and Regulatory Policy*, 51 FLA. L. REV. 181, 193–94 (1999) (citing off-label uses of cancer drugs and drugs prescribed for healing wounds as instances in which off-labeling has relieved suffering).

60. *See* Gary Young, *FDA Strategy Would Pre-empt Tort Suits*, NAT'L L.J., Mar. 1, 2004, *available at* http://www.law.com/jsp/nlj/PubArticleNLJ.jsp?id=1076428430132.

61. *See FDA Revises Labeling for Doctors; States express Concerns about Preemption*, 74 U.S.L.W. 27, Jan. 24, 2006; Young, *supra* note 60 ("Under the Bush administration, the U.S. Food and Drug Administration (FDA) has adopted a novel legal strategy that would, if successful, leave many consumers claiming injury from pharmaceuticals or medical devices with no recourse to tort law, critics and attorneys charge.").

62. Requirements on Content and Format of Labeling for Human Prescription Drug and Biological Products, 71 Fed. Reg. 3921 (Jan. 24, 2006).

63. *Id.*

64. *Id.; see, e.g.*, Pharm. Res. & Mfrs. of Am. v. Dist. of Columbia. 406 F. Supp. 2d. 56, 65 (D.D.C. 2005).

consumer and the doctor.[65] Several areas in which the FDA claims to categorically preempt state law were listed in the preamble.[66]

One case relied upon by the FDA in supporting its case for preemption, *Buckman Co. v. Plaintiffs' Legal Committee*, implicates off-label prescribing in the context of preemption.[67] The class-action lawsuit alleged that the FDA was defrauded during the approval process for a type of bone screw that was the proximate cause of the plaintiffs' injuries.[68] Two relevant arguments were posited by plaintiffs during the bone screw litigation: that the incentive for fraud was the potential for lucrative off-label

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65. Requirements on Content and Format of Labeling for Human Prescription Drug and Biological Products, 71 Fed. Reg. at 3933–35.

66. *Id.* at 3936. The categories listed are: failure to warn claims against a drug manufacturer when a risk is included in the label but not in the "highlights section" or when risks are not included in an advertisement but are otherwise found in the labeling; failure to warn claims when the sponsor fails to include contraindications or warnings that are not supported by evidence meeting the standards of the FDA; failure to warn claims for a failure to include in the label or advertisement a statement regarding a risk that has been proposed to the FDA for inclusion but is not required at the time of the claim; failure to warn claims based on the absence of labeling or advertising statements that have been substantively prohibited by the FDA in such a format; and claims that a pharmaceutical company breached an obligation to the plaintiff based on statements approved by the FDA unless the FDA finds that the company withheld material information relating to the statement. *Id.*

67. Buckman Co. v. Plaintiffs' Legal Comm., 531 U.S. 341 (1998). The plaintiff in this case alleged that the defendant pharmaceutical company misrepresented material facts as to the usage of its medical device, bone screws, when it applied to the FDA for approval and that the FDA would not have approved the bone screws for sale had the FDA been apprised of such material facts. More concisely put, but for defendant's misrepresentation, the plaintiffs would not have been injured because the bone screws would not have been approved for sale. *Id.*

68. *Id.* at 348.

> We hold that the plaintiffs' state-law fraud-on-the-FDA claims conflict with, and are therefore impliedly pre-empted by federal law. The conflict stems from the fact that the federal statutory scheme amply empowers the FDA to punish and deter fraud against the Agency, and that this authority is used by the Agency to achieve a somewhat delicate balance of statutory objectives. The balance sought by the Agency can be skewed by allowing fraud-on-the-FDA claims under state tort law.

Id.

prescribing, and that the manufacturer was aware that the product would be used for other purposes than those approved in its New Medical Device Application.[69] The Court held that Congress intended to empower the FDA to address fraud against the agency and that state tort suits alleging fraud on the FDA interfered with that power.[70] The Court's finding that fraud on the federal government was impliedly preempted by the FDA is relevant in the context of pharmaceuticals not only because it suggests that the Court is receptive to "implied preemption" arguments, but also because it applies such logic in the context of off-label prescriptions.[71]

II. PHARMACOGENOMICS- A UNIQUE SPECIES OF DRUGS

A. What is at Stake?

Pharmacogenomics not only represents advances in actual drug therapy, it represents the promise of efficiency in drug trials and treatment.[72] The actual cost of drug development is debated: some suggest that drug development for FDA approval costs close to $100 million while others argue that the cost during drug development alone is close to $400 million per drug.[73] Additionally, it is estimated that the total time between the start of drug development to market is close to 180 months.[74] The identification of gene variations in drug metabolism will allow researchers to narrow drug trials according to a particular genotype, rather than testing on diverse

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69. *Id.* at 341.

70. *Id.* at 348.

71. *Id.*

72. Human Genome Project, *supra* note 1.

73. At present, the cost of drug research and development is disputed. Public Citizen, a consumer advocacy group suggests that research and development costs only $110 million to obtain FDA approval. However, the Tufts Center for the Study of Drug Development argues that the expenditures from the development period are around $400 million per approved drug and the total capitalized cost is generally around $800 million per approved drug. DiMasi, *supra* note 15.

74. Oldham, *supra* note 6 (arguing that while the actual drug approval time has decreased, the development time has increased).

populations and genotypes.[75] One commentator observes that it is prohibited by federal regulation for the IRB to approve a clinical trial that would expose a subject to a known risk; thus, future researchers may not have the choice to include a more random group of subjects.[76] Others are concerned that this will lead to less accurate trials and inferior understanding of drugs.[77]

While pharmacogenomics could potentially save a pharmaceutical company money in research and trials, it may cost them in revenue.[78] Drugs that are designed for a specific genotype are unlikely to produce the "blockbuster effect" or commercial demand of drugs aimed at the general population.[79] Off-label prescribing could provide additional revenue for a company producing genotype specific drugs,[80] but this practice seems inherently more dangerous due to the limited availability of facts to predict the general public's response to the drug. Additionally, pharmacogenomics creates an increased risk of disparity in treatment among genotypes.[81] The possibility of pharmaceutical companies focusing pharmacogenomic drug development on more common genotypes is a concern.[82]

Despite the promise of pharmacogenomics, an array of continuing and novel concerns will arise as the FDA is faced with the task of approving

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75. Mark A. Rothstein & Phyllis Griffin Epps, *Ethical and Legal Implications of Pharmacogenomics*, 2 NATURE REVIEWS GENETICS 228 (2001)..

76. Tilo Mandry, *Legal Implications of Pharmacogenomics Regarding Drug Trials, Drug Labeling, and Genetic Testing for Drug Prescription: An International Approach*, 59 FOOD & DRUG L.J. 519, 523 (2004).

77. *See* Rothstein & Epps, *supra* note 75 at 228.

78. When drugs are made with a specific population, in this case a genotype, in mind, it is unlikely that they will have the "blockbuster" effect of drugs presently on the market. Rothstein, *supra* note 75, at 228–29; *see also* DiMasi, *supra* note 15.

79. *See* Rothstein & Epps, *supra* note 75, at 228–29.

80. *But see* Phyllis Griffin Epps, *White Pill, Yellow Pill, Red Pill, Brown Pill: Pharmacogenomics and the Changing Face of Medicine*, HEALTH L. PERSP. May 30, 2000, *http*://www.law.uh.edu/healthlaw/perspectives/genetics/20000530Whitepill.html (noting that the Orphan Drug Act creates incentives for drug manufacturers to research and develop drugs for rare diseases through tax credits and exclusive marketing rights).

81. Rothstein & Epps, *supra* note 75; *see generally* Epps, *supra* note 80.

82. Rothstein & Epps, *supra* note 75; *see generally* Epps, *supra* note 80.

pharmacogenomic drugs. It is inevitable that there will be problems in the regulation of pharmacogenomics. For example, limited trials will yield limited data,[83] which may prove dangerous especially in the context of off-label prescriptions. But to disallow off-label prescriptions is "paternalistic" and could be devastating to the people who rely on the availability of off-label drugs.[84] Other problems may include disinterest by the pharmaceutical companies as the financial incentive is minimal and the possibility of liability is great, they may decline to produce drugs that are genomically engineered, preferring "blockbuster," one-size-fits-all drugs.[85] Finally, the already realized problem of the FDA's weak post-market surveillance will undoubtedly hinder pharmacogenomics as many of the uncertainties of pharmacogenomics will be discovered only after the approval process.[86]

B. FDA and Pharmacogenomic Drug Development

The FDA has taken steps to anticipate the development of pharmacogenomics. In 2003, the FDA published a draft guidance document for public comment followed by the publication of guidance regarding pharmacogenomics role in data submissions in March of 2005.[87] The 2003 draft proposal included definitions by which drug companies or sponsors are to classify their submitted data, and developed algorithms requiring sponsors to submit data obtained in the Investigative New Drug Application stage if it later will be used to enroll or exclude persons from a trial.[88] In the INDA

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83. *See* Rothstein & Epps, *supra* note 75, at 228 ("A group that reflects the diversity of the population yields information on how a drug will behave in a greater number of people. If the clinical trial group is smaller, or is less genotypically diverse, there is a greater risk that some side effects will go undetected.").

84. *See* Beck & Azari, *supra* note 56, at 76–85.

85. Rothstein & Epps, *supra* note 75, at 229 ("Incentives for pharmaceutical companies to invest time, effort and resources into the development of drugs to treat limited populations are few . . . .").

86. *Id.*

87. Michelle Meadows, *Genomics and Personalized Medicine*, FDA CONSUMER MAGAZINE, Nov.-Dec. 2005, *available* at: http://www.fda.gov/fdac/features/2005/605_genomics.html (explaining that presently pharmacogenomic data are considered research and exploratory in nature and are not required to be submitted).

88. Woodcock, *supra* note 1, at 95–97.

stage, the FDA has developed a structure in which the applicant may confidentially report his pharmacogenomic findings through the Voluntary Genomic Data Submission (VGDS).[89] Included in submissions, the FDA requests: a full clinical study report providing a clear explanation of the critical design features of the study; information on the methods used to implement the study; relevant individual patient data; any protocol deviations; individual adverse events; pharmacogenomic and other biomarker datasets; and correlations between the clinical and pharmacogenomic data.[90] The FDA envisions a system in which the agency, researchers, and drug companies work together to gather data to advance pharmacogenomics.[91]

In terms of labeling, the FDA anticipates that as genetic tests become more common, information regarding genotype may begin to appear on labels to add a predictive value as to how a particular patient will metabolize a drug.[92] Eventually the FDA predicts that pharmacogenomic labels will include directions to doctors in terms of which genetic tests to run prior to prescription.[93] At present there exists at least one example of such labeling. A leukemia drug includes in its label an alert to doctors regarding a test for

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89. *Id.* at 96–97.

90. U.S. FOOD & DRUG ADMIN., GUIDANCE FOR INDUSTRY, PHARMACOGENOMIC DATA SUBMISSIONS 8–9 (2005), *available at* http://www.fda.gov/cder/guidance/6400fnl.pdf.

91. *See* U.S. FOOD & DRUG ADMIN., INNOVATION OR STAGNATION: CHALLENGE AND OPPORTUNITY ON THE CRITICAL PATH TO NEW MEDICAL PRODUCTS (2004), http://www.fda.gov/oc/initiatives/criticalpath/whitepaper.html. The FDA has explained how pharmacogenomics can be advanced:

> The product development problems we are seeing today can be addressed, in part, through an aggressive, collaborative effort to create a new generation of performance standards and predictive tools. The new tools will match and move forward new scientific innovations and will build on knowledge delivered by recent advances in science, such as bioinformatics, genomics, imaging technologies, and materials science.

Id.

92. Woodcock, *supra* note 1, at 98–99.

93. *Id.* at 99.

certain genetic variants considered to respond adversely to the drug.[94] However, this particular label does not require such testing prior to prescription.[95]

III. PAST LEGISLATIVE RESPONSES TO DRUG DEVELOPMENT OBSTACLES

A. Responses to Drug Shortages and the Tort System

While the FDA approval process represents a regulatory approach to advancing public health, some consider the threat of lawsuit to be an effective protection for public health and safety.[96] The tort system relies on individual patients bringing lawsuits for individual harms to deter future risky acts through threat of economic sanction.[97] A general criticism of the tort system is that only a small percentage of persons bringing suits have actually been injured, which results in a system that fosters excessive treatments and tests ordered by doctors, which do not enhance the quality of a patient's care.[98] Drug companies seek to offset the risk of costly lawsuits through selectivity in drug development.[99] This may result in a drug

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94. Susanne Haga & Wylie Burke, *Using Pharmacogenetics to Improve Drug Safety and Efficacy,* 291 JAMA 2869, 2869–70 (2004).

95. *Id.* at 2870. Michelle J. White, *The Value of Liability in Medical Malpractice*, 82 HEALTH AFFAIRS 75 (1994).

96. *See* White, *supra* note 95, at 75.

97. *See* James R. Copland, *A Message from the Director, The Lawsuit Industry's Effect on American Healthcare*, TRIAL LAWYERS, INC., HEALTH CARE, 2005, *available at* http://www.triallawyersinc.com/healthcare/hc01.html.

98. Barbara J. Evans & David A. Flockhart, *The Unfinished Business of U.S. Drug Safety Regulations,* 61 FOOD & DRUG L.J. 45, 52.

> Unsafe prescribing practices may go unpunished even as prudent ones draw large penalties. The tort system provides a "fragmented and capricious response" to injuries. Effective deterrence requires precision: those claims—and only those claims—that involve a negligent injury should be compensated. Lacking this precision, drug injury lawsuits are not a strong compliance mechanism.

Id.

99. *See* Epstein, *supra* note 8, at 757–58.

company choosing not to develop effective drugs due to the possibility that they could lose economic viability after lawsuits.[100] While deterring negligent practices within the medical and pharmaceutical industry is a benefit of the tort system, the risk of deterring drug development and innovative medical care is a disadvantage.

The National Childhood Vaccine Injury Program was developed due to concerns that pharmaceutical companies derive little revenue from vaccines and that an onslaught of lawsuits threaten the nation's vaccine supply.[101] The program may be viewed as a type of tort reform driven by a public health necessity.[102] Another tort shield for pharmaceutical companies is the learned intermediary doctrine.[103] A doctor who prescribes a particular drug owes several duties to her patient and can be held liable if she fails to abide by those duties.[104] The learned intermediary doctrine provides that pharmaceutical companies have no duty to warn a consumer of the dangers of the drug so long as adequate warning was provided to prescribing physicians.[105] The doctrine is based on a theory that the doctor is in the best position to evaluate the information provided by the manufacturer concerning the risks and benefits of its drug and to evaluate the individual needs and susceptibilities of the patient.[106]

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100. Copland, *supra* note 97.

101. About the National Vaccine Injury Compensation Program, http://www.usdoj.gov/civil/torts/const/vicp/about.htm (last visited Feb. 22, 2008).

102. *Compensating Vaccine Injuries: Are Reforms Needed?: Hearing Before the Subcomm. on Criminal Justice, Drug Policy, & Human Res. of the H. Comm. on Gov't Reform*, 106th Cong. 106–07 (1999) (statement of Thomas E. Balbier, Jr., Director, National Vaccine Injury Compensation Program).

103. 63A AM. JUR. 2D *Products Liability* § 1200 (2008).

104. *Id.*; *see also* 3 STEVEN E. PEGALIS, AMERICAN LAW OF MEDICAL MALPRACTICE § 17:9 (2005). First, a doctor must make an accurate diagnosis, have a full drug history and be familiar with the drug actions and any potential drug interactions. The doctor must also use reasonable care in the manner in which she prescribes the medication, and has a duty to advise the patient of the diagnosis made and the medications prescribed, including their risks and side effects. *Id.*

105. 63A AM. JUR. 2D *Products Liability* § 1200 (2008).

106. Diane Schmauder Kane, Annotation, *Construction and Application of Learned-Intermediary Doctrine*, 57 A.L.R. 5TH 1, § 2[a] (1998).

Similarly, preemption by the FDA of lawsuits based on labeling limits the availability of tort remedies for injured persons,[107] subsequently protecting the manufacturer and shielding doctors from claims alleging failure to adequately inform of risk information.[108] Whether the reach of the FDA's preemption is as broad as its ambition is unclear. Preambles to final rules are allotted a limited amount of deference;[109] the FDA argues implied preemption in prescription drug labeling as Congress has not explicitly granted the FDA such preemptive authority.[110]

Nevertheless, prior to the FDA's inclusion of preemption language in any of its regulations, courts have been willing to recognize FDA preemption.[111] The FDA has submitted various amicus briefs in support of defendant pharmaceutical companies claiming that FDA regulations preempt state law in matters of drug labeling.[112] Recently, a federal trial court

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107. *See generally* MARGARET H. CLUNE, CTR. FOR PROGRESSIVE REFORM, STEALTH TORT REFORM: HOW THE BUSH ADMINISTRATION'S AGGRESSIVE USE OF THE PREEMPTION DOCTRINE HURTS CONSUMERS 1 (2004), *available at* http://www.progressiveregulation.org/articles/preemption.pdf; Allison Zieve & Brian Wolfman, *The FDA's Argument for Eradicating State Tort Law: Why It Is Wrong and Warrants No Deference*, 21 Toxic L. Rep. (BNA) 516 (May 25, 2006).

108. *See* Young, *supra* note 59.

109. *See* U.S. CONST. amend. VI, § 2. The Supremacy Clause of the United States Constitution establishes that federal law "shall be the supreme Law of the Land; and the Judges in every State shall be bound thereby, any Thing in the Constitution or Laws of any State to the Contrary notwithstanding." *Id.* This is defined as prohibiting state law from interfering with or establishing laws contrary to those of Congress. *See* Gibbons v. Ogden, 22 U.S. 1 (1824). However, those opposing FDA preemption also argue that courts should give little deference to preamble language. Preambles cannot impose legal requirements, and therefore do not carry the force of law. *See* Zieve & Wolfman, *supra* note 107, at 10.

110. Requirements on Content and Format of Labeling for Human Prescription Drug and Biological Products, 71 Fed. Reg. 3922, 3934 (Jan. 24, 2006) (to be codified at 21 C.F.R. pts. 201, 314 & 601).

111. *See* Hillsborough County v. Automated Med. Labs., Inc., 471 U.S. 707, 714 (1985) (citing Chevron U.S.A., Inc. v. Natural Res. Def. Council, Inc., 467 U.S. 837, 842–45 (1984)) (holding that in the absence of expressed congressional intent, the scope of the FDA's preemptive authority is determined by the FDA's position).

112. Requirements on Content and Format of Labeling for Human Prescription Drug and Biological Products, 71 Fed. Reg. at 3935.

opinion addressed the issue of preemption directly in a failure-to-warn suit, a tort suit based on a drug manufacturer's failure to include a suicide warning on the label of certain drugs.[113] The FDA supported the defendant by submitting an amicus brief.[114] The holding turned on the authority of the FDA to regulate drugs. The court found that through the FDCA, Congress had granted the FDA the power to regulate "the specifics of drug labeling, making important judgments of what is required for safety of the consuming public, what new drugs may appear in the marketplace, and what warnings their instructions and labels must carry."[115] The court noted that the Supreme Court gives deference to an agency's own interpretation of the statute and regulations[116] and that preemptive intent may be inferred from amicus briefs.[117]

Since the publication of the new labeling rule, courts have been divided on how much weight to afford the preemption claims in the preamble. In *In re Bextra and Celebrex Marketing Sales Practices and Product Liability Litigation*, the U.S. District Court for the Northern District of California dismissed a failure-to-warn claim based on state tort law against a drug company reasoning that the FDA had implied authority to determine whether state laws conflict with FDA regulations due to its authority over drug safety delegated by Congress.[118] However, in *McNellis v. Pfizer, Inc.*, a federal district court in New Jersey declined to give deference to the FDA's preamble and determined that New Jersey failure-to-warn claims were not in conflict with the FDA regulations.[119] A petition for certiorari from a Second Circuit Court of Appeals decision, affirming a finding of summary judgment for the defendant because petitioner's claims

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113. Colacicco v. Apotex, Inc., 432 F. Supp. 2d 514 (E.D. Pa. 2006).

114. Brief for the United States as Amicus Curiae at 1, Colacicco v. Apotex, Inc., 432 F. Supp. 2d 514 (E.D. Pa. 2006) (No. 05-5500).

115. *Id.* at 518.

116. *Id.* at 525.

117. *Id.*

118. *See In re* Bextra & Celebrex Marketing Sales Practices & Prod. Liab. Litig., No. M: 05-1699 CRB, 2006 WL 2374742 (N.D. Cal. Nov. 19, 2007).

119. *See* McNellis *ex rel.* DeAngelis v. Pfizer, Inc., No. Civ. 05-1286 (JBS), 2006 WL 2819046 (D.N.J. Sept. 29, 2006).

were preempted, was heard by the Supreme Court this term.[120] The factual underpinnings of the case involve a medical device and the issue before the Court is whether the Medical Device Act's express preemption provision is a bar to tort claims based on state law.[121] The Court affirmed the ruling of the Court of Appeals, holding that the preemption clause contained in the Medical Device Amendments of 1976 prohibits state tort suits based on the safety of a device that received FDA approval.[122] The Court noted that the preemption clause does not prevent a state from providing a parallel remedy when a claim is based on a violation of FDA regulation.[123] This opinion is not necessarily determinative when considering drugs since the Medical Device Act includes an express preemption clause,[124] whereas the FDCA does not include one. Instead, its preemption claim is based on implied or field preemption. However, it is noteworthy that Justice Scalia, writing for the majority, directly addresses the dissent's contention that tort lawsuits are permitted in the case of drugs. Justice Scalia dismissed this contention as "assumed" and "by hypothesis."[125]

B. Responses to Lulls in Drug Development

When drugs were not being produced for 'orphan diseases' because of the lack of financial incentive to create drugs for small populations, a helpful response to the problem was created by the Orphan Drug Act of 1983 (ODA).[126] The Act was passed with the goal of spurring the pharmaceutical industry into developing drugs to treat rare diseases, which are those affecting fewer than 200,000 Americans.[127] Also covered by the ODA are drugs with high development costs that are unlikely to be recouped

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120. *See* Riegel v. Medtronic, Inc., 128 S. Ct. 999 (2008).

121. *Id.*

122. *Riegel*, 128 S. Ct. 999 (2008).

123. *Id.*

124. 21 U.S.C. § 360k(a) (2000).

125. *Riegel*, 128 S. Ct. 999 (2008).

126. Orphan Drug Act, Pub. L. No. 97-414, 96 Stat. 2049 (1983) (codified as amended at 21 U.S.C. §§ 360aa-360ee (2000)).

127. 21 U.S.C. § 360ee(b)(2)(1)(A) (2000).

by sales in the United States.[128] If an NDA for an orphan drug is approved, the FDA may not approve NDAs for the particular orphan drug from other applicants until seven years from the date of original approval.[129] In addition to the reward of market exclusivity for seven years, the ODA provides research grants and tax credits to pharmaceutical developers working in the area.[130] Ongoing studies receive priority in funding while the remainder of available funds is awarded to new studies.[131] On average, the Office of Orphan Product Development funds between twelve and fifteen new studies per year.[132] The ODA provides an effective means to reach its goal of drug development for rare diseases: by 2003, over 250 treatments for orphan diseases were approved in the United States contrasted to the mere ten that had been developed prior to the ODA.[133]

C. Recent Legislative Efforts

After several high profile lawsuits stemming from 2004 drug withdrawals, and Congress passing to Democratic control in 2006, the present political climate became conducive to reforms aimed at the FDA's failure to adequately follow the safety of approved drugs.[134]

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128. *Id.* § 360ee(b)(2)(1)(B).

129. *Id.* § 360cc(a); *but see id.* § 360cc(b)(1) (stating that if the Secretary of Health and Human Services finds that the approved entity cannot assure the availability of sufficient production of the drug, then after notice and opportunity to respond is given to the approved applicant, the Secretary may approve the approval of another NDA for the same orphan disease prior to the expiration of seven years).

130. Frequently Asked Questions Concerning the OOPD Grant Program, http://www.fda.gov/orphan/grants/faq.htm (last visited Jan. 27, 2007) (indicating that per annum clinical trials for orphan drugs are presently awarded grants not exceeding $200,000 during Phase I, and grants equaling up to $350,000 during Phases II and III).

131. *Id.*

132. *Id.*

133. Carlos Rados, *Orphan Products, Hope For People with Rare Diseases*, FDA CONSUMER MAGAZINE, Nov.-Dec. 2003, *available at* http://www.fda.gov/fdac/features/2003/603_orphan.html.

134. Jeffrey Young, *Democratic Leaders Eye FDA Reforms*, THE HILL, Nov. 16, 2006, at 11, *available at* http://www.thehill.com/thehill/export/TheHill/News/TheExecutive/111606_fda.html.

Previously, Senator Grassley introduced the "Food and Drug Administration Act of 2005,"[135] which proposed the establishment of a "Center for Postmarket Drug Evaluation and Research" within the FDA. The "Center for Postmarket Drug Evaluation and Research" was authorized to require post-market surveillance of approved drugs by drug companies, to study the results of postmarket surveillance programs, to make information from such studies available to the public through publication in the Federal Register and on a website, and to take appropriate action when a drug presents an unreasonable risk.[136] Akin to a cost-benefit analysis, the determination of an unreasonable risk would be determined by "the risk in relations to the known benefits of such drug or biological product."[137]

Similarly, Senators Enzi and Kennedy introduced the "Enhancing Drug Safety and Innovation Act of 2006," which would require pharmaceutical companies to create a Risk Evaluation and Management Strategy (REMS). The REMS plan would include a requirement of regular reports on adverse events involving new drugs, include yearly reviews for the first three years after approval of a drug, and give the FDA the ability to require post-market clinical trials and studies by the pharmaceutical companies to penalize non-compliance.[138] The results from Phase III and Phase IV clinical trials would be publicly posted.[139] Finally, the legislation would create a Drug Safety Oversight Board to handle disputes between drug companies and the FDA, as well as create the Reagan-Udall Institute for Applied Biomedical Research to study proposals to reduce the time for new drug approval.[140]

The bill that ultimately passed, the FDAA, re-authorized the collection and spending of user fees by the FDA to expedite drug approval and to continue monitoring prescription drugs once they are approved and enter the market.[141] The FDAA requires the registration of all clinical trials

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135. S. 930, 109th Cong. (2005).

136. *Id.* sec. 2(a), § 507(b)(1) (amending 21 U.S.C. § 351).

137. *Id.*

138. S. 3807, 109th Cong. sec. 101, § 505(o) (2006) (amending 21 U.S.C. § 355).

139. *Id.* sec. 101, § 505(o)(4)(c) (amending 21 U.S.C. § 355).

140. *Id.* sec. 101, § 505(o)(2)(E) (amending 21 U.S.C. § 355).

141. *See* Food and Drug Administration Amendments Act of 2007, Pub. L. No. 110-85, sec. 801(a), § 402, 121 Stat. 823, 904–20.

and the publication of clinical trial results for approved drugs and devices.[142] Drug applicants must now also include study result in a results data bank, which will be available to the pubic on the internet.[143] The FDA is also authorized to order post-approval studies or clinical trials of a drug when new safety information is present.[144] Yet, this power is not unlimited, as the FDA may require a post-market approval study only after it becomes aware of new safety information and determines that the existing post-market surveillance of the drug is insufficient.[145] The FDA may also order a label change when it believes that new safety information should be included in the drug label.[146] However, the pharmaceutical company is permitted to provide its recommendations for changes to the labeling or to submit its argument for why changes are unnecessary.[147] Only after discussions with a pharmaceutical company regarding its resistance to a label change may the FDA order a label change, which may then be appealed.[148] A Risk Evaluation and Mitigation Strategies (REMS) plan may also be required by the FDA.[149] When deciding whether a REMS plan is necessary, the FDA evaluates a number of factors, including the size of the population that will use the drug, the seriousness of the condition treated by the drug, the expected benefit of the drug, the duration of treatment, the seriousness of known adverse events, and whether the drug is a new molecular entity.[150] The FDA is also required to develop post-market risk identification and analysis methods.[151] A REMS plan must be submitted by the

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142. *See id.*

143. *Id.*

144. *Id.* sec. 901(a), § 505, 121 Stat. at 922–26.

145. *See id.* sec. 901(b), § 505-1, 121 Stat. at 926–38.

146. *Id.* sec. 901(a), § 505, 121 Stat. at 922–26.

147. *Id.*

148. *Id.*

149. *Id.* sec. 901(b), § 505-1(a)(1), 121 Stat. at 926.

150. *Id.*

151. *Id.* sec. 901(b), § 505-1(a)(2)(B), 121 Stat. at 927.

pharmaceutical company within 120 days of notice by the FDA.[152] The REMS plan must include assessments at eighteen months, three years, and seven years.[153] Additionally, a REMS plan may suggest that healthcare practitioners have specialized training, patients enroll in a registry, and that a medication guide and patient package insert be developed.[154] Failure of drug companies to comply with any of these new requirements can result in fines.[155]

IV. APPLICABILITY OF PAST RESPONSES TO PHARMACOGENOMICS

A. Preemption

The FDA's case for preemption is compelling in the context of pharmacogenomics. However, the past shortcomings of the FDA's post-approval surveillance support the argument that tort suits may be necessary as an additional check on drugs in the marketplace and as a means to compensate those who are injured by such drugs.[156] It is extreme to pass legislation that virtually eliminates the possibility of compensation for drug injury victims.[157]

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152. *Id.* sec. 901, § 379g(iv), 121 Stat. at 927.

153. *Id.*

154. *Id.* sec. 901(b), § 505-1(d), 121 Stat. at 929.

155. Food and Drug Administration Amendments Act of 2007, Pub. L. No. 110-85, sec. 801(a), § 402, 121 Stat. 823, 904–20.

156. *See* Allison Zieve & Brian Wolfman, *The FDA's Argument for Eradicating State Tort Law: Why It Is Wrong and Warrants No Deference*, 21 TOXIC L. REP. (BNA) 516, 517 (May 25, 2006).

157. Gary Young, *FDA Strategy Would Pre-Empt Tort Suits*, NAT'L L.J., Mar. 1, 2004, http://www.law.com/jsp/nlj?PubArticlePrinterFriendlyNJL.jsp?id=1076428430132.

> Under the Bush administration, the U.S. Food and Drug Administration (FDA) has adopted a novel legal strategy that would, if successful, leave many consumers claiming injury from pharmaceuticals or medical devices with no recourse to tort law, critics and attorneys charge. That strategy is pre-emption, basically

Opponents to the FDA's preemption policy argue that there is no direct conflict between a suit for damages and the regulatory requirements of drug labeling.[158] Often, labels are inadequate and must be changed after approval; thus, the label is not a final decision. Rather, they are adjusted with time and are developed through negotiation with the pharmaceutical company.[159] In the context of pharmacogenomics, there is much concern that lawsuits would be a powerful deterrent to actual drug development. Since the profitability of pharmacogenomics is unknown, lawsuits for damages against a pharmaceutical company may result in the removal of some effective drugs from the market by pharmaceutical companies.[160] Also, there is the possibility that a pharmaceutical company may refuse to do research for future pharmacogenomic drugs because of the high risk and low return of the drugs.[161] This directly implicates the FDA's mission to provide for safe, effective drugs to reach the market.[162] While such concerns are reasonable, efforts to reform tort law may be more helpful than denying an injured party judicial recourse.[163] Although tort suits may explain some industry reluctance in producing certain drugs, they do not necessitate such drastic measures by the FDA under questionable authority. Methods to

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> nullification of state actions that conflict with or supplement FDA decision.

Id.

158. Zieve & Wolfman, *supra* note 156, at 519. "And 'there is no general inherent conflict between federal pre-emption of state [regulatory] requirements and the continued vitality of state common-law damages actions.' In other words, a verdict ordering the payment of damages does not require a drug manufacturer to do anything inconsistent with any FDA requirement." *Id.*

159. *Id.*

160. *See* Rothstein & Epps, *supra* note 75, at 229 ("Without the opportunity to recoup their investment, drug companies will not continue their efforts.").

161. *Id.*

162. FDA's Mission Statement, http://www.fda.gov/opacom/morechoices/mission.html (last visited Feb. 25, 2008).

163. *See* JOINT ECON. COMM., 104TH CONG., IMPROVING THE AMERICAN LEGAL SYSTEM: THE ECONOMIC BENEFITS OF TORT REFORM (1996), *available at* http://www.house.gov/jec/tort/tort/tort.htm.

counter such outside influences must be developed to ensure that new drug development is not curtailed by fear of lawsuits.

Tort suits may provide a valuable means for individuals to receive compensation for injury and may ensure that pharmaceutical companies are alert and responsive to potential safety issues.[164] While the FDA argues that too much label information may result in confusion and individuals failing to take advantage of available drugs, perhaps increased information is necessary and value should be placed on the individual's choice to use or not to use a drug rather than on the FDA's apparently imperfect judgment.[165]

B. Orphan Drug Laws

Some of the benefits of the Orphan Drug Act (ODA) may be helpful in encouraging drug companies to devote more time and effort into the field of pharmacogenomics but awarding exclusive patents is unacceptable in the field of pharmacogenomics.[166] While this is a new area and concerns about profit may abound for pharmaceutical companies, the advantages of these drugs[167] and the mission of the FDA to ensure availability preclude such an option. More important is the availability of multiple options for all persons and genotypes and this is better accomplished through the availability of many treatment options rather than the exclusion of later developed drugs.[168]

The use of tax credits and research grants may be useful as an incentive for those who contribute data through Voluntary Genomics Data Submissions (VGDS). At present, the FDA suggests an incentive of providing such information are time and cost saving benefits that will occur by familiarizing the FDA and the drug company with new approaches to

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164. *See generally* Zieve & Wolfman, *supra* note 156, at 518.

165. *See generally* Epstein, *supra* note 8, at 748 ("[T]here is no reason to place trust in a government monopoly, especially one that has shown itself to rate false positives (letting drugs that should be kept off the market onto the market) more highly than false negatives (keeping drugs off the markets that should be allowed). Since warnings are not coercive but informative, there is no need for a government monopoly.").

166. Rothstein, *supra* note 75, at 229 ("The United States and Japan have enacted legislation to stimulate research and the development of orphan drugs through market mechanisms, such as tax-based cost incentives and time-limited monopolies, with varying degrees of governmental intervention.").

167. *See supra* text accompanying note 4.

168. *See* Epstein, *supra* note 8.

pharmacogenomics and thereby avoiding future delays during review.[169] Also, the FDA suggests that this creates an opportunity for sponsors to impact the FDA's position thereby building consensus for future pharmacogenomic policies.[170] At the close of 2006, approximately twenty submissions had been made to the VGDS, which according to the FDA "varied significantly in terms of content and focus."[171] The necessity of "standardization in data generation, normalization and submission" and "measures of data quality" became apparent through these submissions.[172] As the process for better voluntary submissions is developed, the administrative burden of detailing voluntary submissions may be offset by the possibility of additional benefits in research grants.

The opportunity for discrimination is also of concern when considering whether to adopt similar policies as that of the ODA in the field of pharmacogenomics. When a certain genotype occurs in smaller groups of persons and therefore has a limited market, the possibility exists that drug manufacturers could focus on development for more prevalent genotypes.[173] That a certain genotype exists primarily in a particular race also implicates unique social concerns for drug development and availability.[174] In the development of pharmacogenomics, some scholars suggest that the possibility of drug developers "cherry picking" genotypes to focus their research is possible as "market forces dictate a higher price for the drug."[175] Essentially, a pharmaceutical company realizing the expense of such a drug may be inclined to produce drugs only for populations that are more likely to be able to afford the drug.[176] It will be necessary for legislation to curb such

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169. Genomics at FDA, Voluntary Genomics Data Submission (VGDS), http://www.fda.gov/cder/genomics/VGDS.htm (last visited Jan. 27, 2007).

170. *Id.*

171. Felix W. Frueh, Commentary, *Impact of Microarray Data Quality on Genomic Data Submissions to the FDA*, 24 NATURE BIOTECHNOLOGY 1105, 1106 (2006).

172. *Id.* at 1106.

173. Epps, *supra* note 80.

174. Rothstein & Epps, *supra* note 75, at 228. ("The use of groups in clinical trials that are increasingly similar genotypically raises several important ethical issues regarding social inclusion and adequacy of current regulatory frameworks.").

175. *Id.* at 229.

176. *Id.*

practices by creating a system to track potential discrimination and to prohibit federal funding of companies that engage in this behavior.

C. Recent Legislative Responses

Both the Food and Drug Administration Act of 2005 and the Enhancing Drug Safety and Innovation Act of 2006 address the failings of the FDA in post-market surveillance. The bills suggested the establishment oversight boards and authorization of the FDA to require post-market studies by drug companies, and that the public should have access to the information later phases of drug studies.[177] The 2005 bill also maintained the cost-benefit analysis for drug approval decisions.[178] This method may be criticized as devaluing informed decisions made by patients with their doctors as to drug choices. A cost-benefit analysis is ill-suited for pharmacogenomics because the benefit of a drug designed for a particular genotype may be small if quantified in terms of actual people benefited and could therefore be denied entry into the marketplace under this analysis. The determination of an "unreasonable risk" would be determined by "the risk in relations to the known benefits of such drug or biological product."[179] The 2006 bill is more explicit in developing specific oversight programs for newly marketed drugs, although some criticize that the development of such plans does not elicit sufficient input from patients and providers and that requirements for post-market surveillance should be expanded to include off-label studies.[180] This same criticism can be leveled at the FDAA, because the FDA is limited as to when it can request post-market surveillance and/or REMS plans since it must first identify a new risk. Conversely, this may be a viewed as a method of ensuring that the FDA is not overly paternalistic in its monitoring of drugs and is cautious before ordering expensive trials and studies.

Ultimately, the passage of the FDAA, which includes new tools for monitoring drug safety even after a drug has been approved for sale and new

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177. S. 3870, 109th Cong. (2006).

178. S. 930, 109th Cong. sec. 2(a), § 507(b)(2) (2005).

179. S. 930, 109th Cong. sec. 2(a), § 507(b)(2) (2005).

180. *Building a 21st Century FDA: Proposals to Improve Drug Safety and Innovation: Hearing Before the S. Comm. on Health, Educ., Labor, & Pensions*, 109th Cong. 27 (2006) (statement of Diane E. Thompson, Vice President for Public Policy and Communications, Elizabeth Glaser Pediatric AIDS Foundation).

authority to require label changes, is a step in the right direction for the FDA. However, the FDAA's cost-benefit analysis remains an issue of concern as regards pharmacogenomics. With pharmacogenomics on the horizon, greater emphasis should be focused on providing ready access to advanced drugs by individual consumers, as opposed to level of access produced by cost-benefit analysis. Ultimately, it will be necessary for Congress to re-examine the FDA's mission and to establish more practical methods for attaining its goals by developing drug safety procedures, providing more information to the patient and doctor, encouraging off-label studies, implementing its new post-market surveillance tools in a vigilantly, and forcing all parties involved to bear the responsibility.

V. RECOMENDATIONS FOR THE SUCCESSFUL ENTRY OF PHARMACOGENOMICS

A. A System of Contradictory Aims

Disincentives permeate the health and drug industry from drug approval to marketing and prescribing, the net result being abandonment of quality and distrust by consumers. Concerns arise as to whether the FDA is successfully ensuring that only safe drugs reach the market without unnecessarily keeping effective drugs from those who need them.[181] The success of drug development does not rely simply on production. Rather, it is interwoven into the medical profession and its relationship to the law and governing regulations. Doctors want to reduce the chance of being sued, which can lead to over-treatment, distrust by the patient, and reluctance to share information regarding close-calls or questionable results.[182] Pharmaceutical companies desire profit and are reluctant to expand their drug research once they have obtained FDA approval because knowledge of a new side-effect or "adverse event" resulting from the drug may reduce, or in some cases eliminate, the fruits of their labor in developing the drug.[183] While the FDA's mission is to promote public health, it is not entirely free from pressure as the desire for new drugs affects decision-making.[184] In the

181. *See infra* Part I.

182. *See generally* Copland, *supra* note 97; Fontanarosa et al., *supra* note 7.

183. See Steven Salbu, *Off-Label Use, Prescription, and Marketing of FDA-Approved Drugs: An Assessment of Legislative and Regulatory Policy*, 51 FLA. L. REV. 181, 206-07 (1999).

184. Copland, *supra* note 97.

post-approval timeframe, the FDA's authority is less limited pursuant to the FDAA; but to request a recall or similar halt of drug marketing may bring the FDA's credibility into question.[185] The FDA cannot allow its safety authority to be hindered by bureaucracy in determining the existence of new safety information or for fear that the approval process will seem flawed by such new information.

The FDA's preemption claims may be based in part on its fear that expensive lawsuits will deter further development of drugs.[186] The Center for Drug Evaluation and Research's emphasis on drug development, rather than surveillance, is blamed in part on the user fees set aside for improving approval times, but the past failings in post-surveillance may also be attributed to the lack of authority and recourse that the FDA has once a drug is approved.[187] The mission of the FDA places the agency in an extremely difficult position, as no drugs are 100% safe. Thus, the agency must choose which goal is more important, those that encourage the advancement of drug development and availability, or perhaps the more conservative goals of ensuring that only the safest drugs reach the market. Some respond that the FDA should focus its energies during the approval process for patient-specific therapies on the relative safety of a drug rather than proving its efficacy.[188] Others argue that the FDA standard for drug approval should be legislatively modified to require not only that new drugs are effective but that they are distinct and better than already existing drugs for the same condition.[189]

In the context of pharmacogenomics, this dilemma must be approached differently. Labeling, efficacy, accessibility, and safety issues that complicate the FDA approval process will be further complicated when,

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185. *See* Fontanarosa et al., *supra* note 7.

186. Catherine Struve, *The FDA and the Tort System: Postmarketing Surveillance, Compensation, and the Role of Litigation*, 5 YALE J. HEALTH POL'Y LAW & ETHICS 587, 588 (2005).

187. *Reauthorization of the Prescription Drug User Fee Act: Hearing Before the Subcomm. on Health of the H. Comm. on Energy & Commerce*, 107th Cong. 28 (2002).

188. Oldham, *supra* note 6.

189. *See generally* MARCIA ANGELL, THE TRUTH ABOUT DRUG COMPANIES: HOW THEY DECEIVE US AND WHAT TO DO ABOUT IT (2004) (arguing that there should be price controls in the pharmaceutical industry and that the FDA should revise its rules to require that all new drugs are tested against older patented drugs and only those that are unique and improved should be approved).

for example, pharmacogenomic studies reveal that certain drugs will treat certain genotypes successfully but may not provide any benefit or may have a negative effect on other genotypes. The burden of obtaining FDA approval in addition to the possibility of a lack of economic incentive could be lethal to the development of some pharmacogenomic drugs.[190] Consequently, incentives are necessary to encourage pharmacogenomic research, reporting, and development by drug companies.

One plausible incentive for pharmacogenomic development is through tax credits and research grants similar to those provided by the ODA. In the context of pharmacogenomics, the FDA has stressed its desire to work with researchers and pharmaceutical companies to make these products available.[191] Grants may provide a powerful incentive to encourage contribution in the form of Voluntary Genomic Data Submissions. The increase in submissions will result in an increased understanding by the FDA at earlier stages, thus potentially speeding future approval processes. However, attention must also be focused on ensuring that the benefits of pharmacogenomics are experienced by all genotypes.[192] Lawmakers must be wary of market-driven discrimination. A plan to identify such discrimination and to deter it by withholding incentives is necessary.[193] Already the FDA mandates that all drug manufacturers disclose effectiveness and safety data based on a variety of subgroups including race, sex, and age during the drug development process,[194] and this information

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190. *See generally* Rothstein & Epps, *supra* note 75.

191. *See* U.S. DEP'T OF HEALTH & HUMAN SERVS., FOOD & DRUG ADMIN., INNOVATION OR STAGNATION: CHALLENGE AND OPPORTUNITY ON THE CRITICAL PATH TO NEW MEDICAL PRODUCTS, at iv (Mar. 2004), *available at* http://www.fda.gov.oc/initiatives/criticalpath/whitepaper.pdf ("The product development problems we are seeing today can be addressed, in part, through an aggressive, collaborative effort to create a new generation of performance standards and predictive tools. The new tools will match and move forward new scientific innovations and will build on knowledge delivered by recent advances in science, such as bioinformatics, genomics, imaging technologies, and materials science.").

192. *See* Rothestein & Epps, *supra* note 75

193. *Id.* at 230 ("[I]f consumers must absorb rising pharmaceutical costs, pharmacogenomics will not introduce new questions so much as it will intensify existing ones about equitable access to medical care.").

194. *See* FDA Regulatory Affairs: A Guide for Prescribing Drugs, Medical Devices, and Biologics, *supra* note 6.

should be used not only to study a drug's effects on certain populations but also to monitor potential discriminatory practices in pharmacogenomic drug development.

Post-market surveillance must be strengthened for safety reasons and to restore consumer faith in the FDA, as well as in pharmaceutical companies.[195] Recent legislation has strengthened the FDA's authority to require that pharmaceutical companies follow their products and report their findings, and the FDA should not be hesitant to use this new power.[196] Strategies for passing relevant drug information from the pharmaceutical company and the FDA to the consumers and doctors should be developed. Granting the FDA preemptive authority is not necessary and may expand consumer concerns of impropriety by the FDA in its relationship with drug companies.[197] Rather, tort suits would naturally be curtailed through faster response times by the FDA and faster dissemination of more detailed information regarding the most recent studies and findings related to a particular drug.[198] Patient awareness initiatives should be conducted in addition to making available drug trial and study information. Often it seems that television commercials are one of the few sources of consumer information about new drugs and studies; the availability of drug trial information and other relevant studies will allow consumers to make more informed choices. Not only do consumers deserve to know about drugs that they take, but consumer knowledge may serve to relieve the practice of over-prescribing. Access to information should not only prevent unnecessary

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195. Fontanarosa et al., *supra* note 7, at 2649–50.

196. GAO DRUG SAFETY REPORT, *supra* note 34, at 2.

197. *See generally* Markel, *supra* note 5, at 2491 (finding that the FDA has a high disapproval rating among Americans and must regain their confidence); National Conference of State Legislatures, *FDA Final Rule on Prescription Drug Labeling*, http://www.ncsl.org/statefed/health/fdarule.htm (last visited Mar. 28, 2008) (stating that the preemption provision is contrary to consumer protection goals of the FDA).

198. Karen Barth Menzies, *Preemption and the FDA—Politics as Usual*, ASS'N OF TRIAL LAW. OF AM. (Feb. 2006) ("Essentially, the government's argument [supporting preemption] would create a scenario where manufacturers are encouraged *not* to act quickly in the face of evolving information when a serious safety issue is suspected with a marketed drug. Indeed, manufacturers would be better off to not act at all and simply wait for the FDA to do something."); *see* David M. Fritch, Comment, *Speak No Evil, Hear No Evil, Harm the Patient? Why the FDA Needs to Seek More, Rather than Less, Speech from Drug Manufacturers on Off-label Drug Treatments*, 9 J. MED. & L. 315, 320–21 (2005).

risks for consumers and doctors but reestablish trust at all levels for the patient.

An effective system of post-market surveillance coupled with increased authority to penalize non-compliance is beneficial because it frees up the FDA to move drugs more quickly through the approval process.[199] Such flexibility[200] recognizes the value of drug availability while increased disclosure will serve as a necessary restraint on excessive, uninformed use. Additionally, this increase in information will allow doctors to make intelligent decisions regarding off-label prescribing.[201] In its testimony before the Senate Health, Education, Labor, and Pensions committee, Consumers Union recommended that

> the FDA develop a program to scientifically study drugs widely used in off-label settings. We are not advocating a ban on such use. We are simply asking that some scientific study be brought to this area, so that the labels on these drugs may be expanded and improved in the cases where the scientific evidence is supportive.[202]

Monitoring off-label prescribing will become increasingly necessary as pharmacogenomics become a reality and as data from such off-label monitoring becomes available, it should quickly be made available to doctors and patients.

B. Conclusion

It is necessary for lawmakers to consider current critiques of the FDA and to develop legislation to curb problems with post-marketing surveillance and drug approval. However, such considerations should be made with an eye to encouraging the development of innovative therapies like pharmacogenomics while anticipating their entry into the drug market. Monetary incentives may be necessary, but additional incentives are realized in efforts to reduce the risk of excess tort suits while maintaining a satisfactory approval pace. Preemption is an unnecessary and extreme

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199. GAO DRUG SAFETY REPORT, *supra* note 34, at 5–6.

200. *Hearings*, *supra* note 180, at 25 (statement of Diane E. Thompson, Vice President for Public Policy and Communications, Elizabeth Glaser Pediatric AIDS Foundation) (suggesting that legislation giving the FDA more authority in post-marketing surveillance creates necessary "flexibility" for the Agency).

201. *See generally* Oates, *supra* note 56, at 1274, 1281.

202. *Hearings*, *supra* note 180, at 46 (statement of Jim Guest, President, Consumers Union).

method to ensure drug development and availability at the cost of consumer distrust. A better method includes continued studies, increased communication at all levels, and industry incentives. The first critical step to realizing these goals has been realized by giving the FDA more authority to advance post-market studies of drugs and to respond in various manners to issues that may arise after approval.[203] While this may result in the FDA's ability to act more confidently when approving drugs, it is also necessary to re-establish consumer trust through more access to information. Pharmacogenomics has the potential to revolutionize medicine through individualized treatment plans, but in order to benefit from these drugs, it will be necessary for the legislature to rethink the structure and authority of the FDA and the meaning of its ambitions. In doing so the opportunity for a new and improved relationship between drug companies, the FDA, and consumers exists.

203. GAO DRUG SAFETY REPORT, *supra* note 34, at 5–6.